Amendments to the Drawings:

The attached sheet of drawings includes changes to Figure 1. This sheet replaces original Figure 1.

Attachment: Replacement Sheet (Figure 1).

REMARKS

Reconsideration of the present application in view of the above amendments and the following remarks is respectfully requested.

Claims 1-21 were pending. New claims 23-25 have been added. Accordingly, claims 1-21 and 23-25 are pending. Support for new claims 23-25 may be found in original claims 8 and 10. No new matter has been added via the addition of these new claims.

Claims 1-21 have been amended. Such amendments have been made without acquiescing to the rejections in the Office Action or prejudice to future prosecution of the previously pending claims in a related application. Support for amendments to claims 1 and 16 may be found, for example, in the paragraph bridging pages 4 and 5 and in the second full paragraph on page 5 of WO 03/084976. Claims 2-6, 8-15 and 17-21 have been amended to enter minor changes. Claim 7 has been amended to clarify the claimed subject matter. Support for the amendments to claim 7 may be found in the paragraph bridging pages 4 and 5 of WO 03/084976. No new matter has been added via the above claim amendments.

Election/Restriction

Applicants thank the Examiner for acknowledging Applicants' election with traverse of Group I, claims 1-15, and withdrawing the species restriction set forth in the Restriction Requirement dated November 13, 2006.

Applicants respectfully request reconsideration and withdrawal of the restriction requirement between Group I, claims 1-15 (and new claims 23-25) and Group II, claims 16-21. As indicated above, claim 1 now recites that the liquid phase in which a nucleic acid-containing sample contacts with a nucleic acid binding solid phase and that comprises a source of NH_4^+ or NH_3 has a pH in the range of 8.5 to 9.5. Similarly, claim 16 now recites that the solution in the kit for isolating nucleic acid from a nucleic acid-containing sample comprises a chaotrope and a source of NH_4^+ or NH_3 and has a pH in the range of 8.5 to 9.5. As discussed in detail below, the specific pH range now recited in both method claims (*i.e.*, claims 1-15 and 23-25) and kit claims (*i.e.*, claims 16-21) in combination with the use of NH_4^+ or NH_3, a chaotrope, and a nucleic acid binding solid phase in nucleic acid isolation is novel and inventive. It has been found by the

inventors of the present application that using NH_4^+ or NH_3 and a chaotrope in a solution with a pH in the range of 8.5 to 9.5 in combination with a nucleic acid binding solid phase increases the yield of isolated nucleic acid. Applicants submit that the above-noted novel and inventive feature links the method and kit claims of the present application together. Accordingly, Applicants respectfully request that the restriction between Groups I and II be withdrawn.

Drawings

Applicants thank the Examiner for noting the informality in Figure 1 with respect to the background shading. Applicants submit replacement Figure 1 without the background shading in this figure. Accordingly, Applicants respectfully request that this objection to Figure 1 be withdrawn.

Information Disclosure Statement

It is indicated in the Office Action on page 4 that "[r]eference WO 03/040603 A1 listed on the IDS of 5/10/2007 has been considered only with respect to the abstract, as there was no translation provided."

Applicants note that there is no "WO 03/040603" listed on the IDS of May 10, 2007. It appears that "WO 03/040603" should be WO 03/040364, instead.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-13 and 15 stand rejected under 35 U.S.C. 112, second paragraph, as indefinite. More specifically, it is noted in the Office Action that claim 1 and its dependent claims (*i.e.*, claims 2-15) recite "providing a source of NH_4^+ or NH_3" in step (c) but also recites "a liquid phase comprising the chaotrope and the NH_4^+ or NH_3" in step (d). It is unclear to the Patent Office whether the NH_4^+ or NH_3 recited in step (d) of claim 1 is limited to NH_4^+ or NH_3 *per se*, or whether it also includes a "source of NH_4^+ or NH3," such as urea, which is a common chaotropic agent. It is further noted that claim 14 specifies the source of NH_4^+ or NH_3 to be a solution of ammonia, thus clarifying the issue, but only for that claim.

Applicants have amended step (d) of claim 1 to read " a liquid phase comprising the chaotrope and the source of NH_4^+ or NH_3." Accordingly, the terms used in steps (c) and (d) of claim 1 now are consistent.

Claims 7-12 stand rejected under 35 U.S.C. 112, second paragraph, as indefinite. More specifically, claims 7 and 9 and their dependent claims (*i.e.*, claims 8 and 10, respectively) recite "wherein the nucleic acid . . . ." It is unclear to the Patent Office whether this language refers to the nucleic acid to be isolated or to the nucleic acid contained in the sample.

Applicants have amended claim 7 to recite "wherein the nucleic acid to be isolated . . . ." Accordingly, the ambiguity associated with "the nucleic acid" in claim 7 has been eliminated.

In view of the above remarks, Applicants submit that this ground of rejections under 35 U.S.C. 112, second paragraph, has been overcome. Applicants respectfully request that these rejections be withdrawn.

Claim Rejections Under 35 U.S.C. § 102

Claims 1-15 stand rejected under 35 U.S.C. 102(b) as anticipated by Kuroita *et al.* (U.S. Patent No. 5,990,302, referred to below as "Kuroita") as evidenced by Alleman (Free Ammonia-Nitrogen Calculator & Information [online], 24 December 1998, [retrieved on July 18, 2007], retrieved from the internet: <cobweb.ecn.purdue.edu/~piwc/w3-research/free-ammonia/nh3.html>).

To facilitate allowance and without acquiescing to the rejection in the Office Action, Applicants have amended claim 1 to specify that the liquid phase in which a nucleic acid-containing sample contacts with a nucleic acid binding solid phase and that comprises a chaotrope and a source of NH_4^+ or NH_3 has a pH in the range of 8.5 to 9.5. This specified pH range or an exemplary pH that falls within this range is not disclosed in Kuroita. Kuroita relates to a method for isolating a ribonucleic acid that comprises dissolution of a sample containing the ribonucleic acid (RNA) in an acidic solution containing a lithium salt and a chaotropic agent, bringing the RNA into contact with a nucleic acid-binding carrier, thereby to allow selective adsorption of the RNA alone (*i.e.*, not DNA) onto said carrier, and eluting the RNA from the nucleic acid-bound carrier (*see*, abstract). The acidic solution has a pH not more than 6.0,

preferably 3-4 (*see*, the paragraph bridging columns 4 and 5). Such an acidic solution improved selectivity of the nucleic acid-binding carrier for RNA adsorption and resulted in greater RNA yields (*see*, Example 3, Table 1 and column 10, lines 60-64). Accordingly, Kuroita does not disclose the use of a solution with a pH in the range of 8.5 to 9.5 for contacting a nucleic acid-containing sample with a nucleic acid binding solid phase in a process for isolating nucleic acid as claimed in the present application. In addition, Kuroita relates to methods for isolating RNA only, different from those of the present application that are applicable for both RNA and DNA isolation.

Claims 1, 3-5, 7, 8, 14 and 15 stand rejected under 35 U.S.C. 102(b) as anticipated by Hewitt (EP 0 261 955 A2, referred to below as "Hewitt") as evidenced by Alleman (Free Ammonia-Nitrogen Calculator & Information [online], 24 December 1998, [retrieved on July 18, 2007], retrieved from the internet: <cobweb.ecn.purdue.edu/~piwc/w3-research/free-ammonia/nh3.html>).

As indicated above, Applicants have amended claim 1 to specify that the liquid phase in which a nucleic acid-containing sample contacts with a nucleic acid binding solid phase and that comprises a chaotrope and a source of NH_4^+ or NH_3 has a pH in the range of 8.5 to 9.5. Because Hewitt fails to disclose a solution that comprises a chaotrope and a source of NH_4^+ or NH_3 and has a pH in the range of 8.5 to 9.5, this reference does not anticipate claims 1-15 (and new claims 23-25) of the present application. More specifically, Hewitt relates to a method of preparing DNA bound to a support for hybridization analysis comprising: (A) forming a suspension of source organisms suspected of containing the DNA of interest; (B) treating said organisms with at least one lytic enzyme; (C) degrading proteins in the suspension by digestion with at least one broadly active protease; (D) denaturing said DNA by treatment with alkali metal hydroxide; (E) treating the mixture resulting from step (D) with at least one chaotropic agent; and (F) immobilizing the single-stranded DNA on a support by contacting the mixture resulting from step (E) with said support (*see*, the Disclosure of the Invention section on page 3). Steps (A) to (C) in Hewitt are performed at a pH around 8, although step (A) may be performed in a solution with a pH ranging from about 4 to about 9 (*see*, page 3, lines 29 to page 4, line 46). The sample processed via steps (A) to (C) is then denatured via treatment of an alkali metal hydroxide, preferably NaOH in a preferred concentration range from about 0.1 N to about 1 N (*see*, page 4,

lines 58-61). Such a concentration of NaOH would cause the pH of the solution resulting from step (D) to be above 12. This is consistent with common knowledge in the art that DNA may be denatured using a basic solution with a pH above 11, as evidenced in Luck *et al.*, European Journal of Biochemistry 17(3): 514-522, 1970 (abstract enclosed). Step (E) is performed by adding to the highly basic solution resulting from step (D) a chaotropic agent or a mixture of chaotropic agents. If the chaotropic agent comprises ammonium acetate (an exemplary chaotropic agent in Hewitt), the solution resulting from step (E) may correspond to the liquid phase recited in claim 1 that comprises a chaotrope and a source of NH_4^+ or NH_3 and in which a nucleic acid-containing sample contacts with a nucleic acid binding solid phase. However, Hewitt does not describe the pH of the solution resulting from step (E) in general. In addition, the solutions resulting from step (E) in Examples 1 to 3 in Hewitt all have a pH above 12. Accordingly, Hewitt fails to disclose the liquid phase that comprises a chaotrope and a source of NH_4^+ or NH_3, has a pH in the range of 8.5 to 9.5, and in which a nucleic acid-containing sample contacts with a nucleic acid binding solid phase now recited in claim 1 of the present application.

In addition, as indicated above, Hewitt relates to a method of preparing DNA bound to a support for hybridization analysis. It does not disclose eluting the nucleic acid from the solid phase as recited in claim 2 of the present application.

In view of the above remarks, Applicants submit that this ground of rejections under 35 U.S.C. 102(b) has been overcome. Applicants respectfully request that these rejections be withdrawn.

Claim Rejections Under 35 U.S.C. § 103

Claim 11 stands rejected under 35 U.S.C. 103(a) as unpatentable over Hewitt (EP 0 261 955 A2).

Applicants respectfully traverse this ground of rejection. As discussed above, Hewitt fails to disclose the liquid phase that comprises a chaotrope and a source of NH_4^+ or NH_3, has a pH in the range of 8.5 to 9.5, and in which a nucleic acid-containing sample contacts with a nucleic acid binding solid phase now recited in claim 1 of the present application. Applicants further submit that Hewitt does not suggest or teach one of ordinary skill in the art to modify its teaching to arrive at the claimed invention of the present application.

It has been found by the present inventors that the presence of NH_4^+ or NH_3 in the process for isolating nucleic acid gives an increased yield of nucleic acid compared to cases where NH_4^+ or NH_3 are absent (*see*, the second full paragraph on page 3 of WO 03/084976). Without wishing to be bound by theory, it is thought that the addition of ammonia or ammonium to, for example, the chaotropic binding solution, causes the pH to increase by one unit (*i.e.*, form 7.5 to 8.5). However, the resulting increased yield of isolated nucleic acid is not believed to be purely a pH effect. Simple increase of pH to 8.5 in the absence of ammonia or ammonium does not affect the yield of isolated nucleic acid. However, the pH of the solution in the presence of ammonia or ammonium does have an effect on the increased yield of the isolated nucleic acid. The optimal pH for the step of contacting the sample with the nucleic acid binding solid phase in the presence of ammonia or ammonium is in the range of 8.5 to 9.5 (*see*, the paragraph bridging pages 3 and 4 of WO 03/084976).

Applicants submit that one of ordinary skill in the art would not have modified Hewitt to arrive at the presently claimed invention. From Hewitt to arrive at the presently claimed invention, such a person has to modify Hewitt by selecting ammonium acetate among other chaotropic agents and adjusting the pH in step (E) to be in the range of 8.5 to 9.5. No reasons have been provided in Hewitt for a skilled artisan to do so. First, ammonium acetate is one of four exemplary salts to be used as chaotropic agents with sodium trifluoroacetate as the preferred salt in Hewitt. Second, as discussed above, the solution resulting from step (D) (*i.e.*, denaturing DNA by treating with alkali metal hydroxide) is highly basic. Even assuming that one of ordinary skill in the art happens to choose ammonium acetate as a chaotropic agent for step (E), because ammonium acetate is almost neutral, the addition of ammonium acetate to the solution resulting from step (D) according to step (E) would not significantly change the pH of the solution resulting from step (E). Because Hewitt does not recognize the advantage associated with contacting a nucleic acid sample with a nucleic acid binding solid phase in the presence of ammonia or ammonium and in the optimal pH range of 8.5 to 9.5, one of ordinary skill in the art would not modify Hewitt to arrive at the claimed subject matter of the present application.

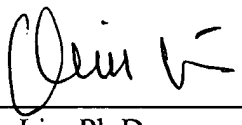
In view of the above remarks, Applicants submit that this ground of rejection under 35 U.S.C. 103 has been overcome. Applicants respectfully request that this rejection be withdrawn.

Applicants believe that the remaining claims of the present application are now allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

The Director is hereby authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Respectfully submitted,

SEED Intellectual Property Law Group PLLC



Qing Lin, Ph.D.
Registration No. 53,937

Enclosures:

Replacement Figure 1
Luck *et al.*, European Journal of Biochemistry 17(3): 514-522, 1970 (abstract)

QXL:kw

701 Fifth Avenue, Suite 5400
Seattle, Washington 98104-7092
Phone: (206) 622-4900
Fax: (206) 682-6031

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Prev Article Next Article

Abstract

Optical Rotatory Dispersion and Circular Dichroism of DNA from Various Sources at Alkaline pH

- *Gerhard LUCK[1],*
- *Christoph ZIMMER[1],*
- *Günther SNATZKE[2] and*
- *Gertrud SÖNDGERATH[2]*

- [1]Zentral-Institut für Mikrobiologie und Experimentelle Therapie der D.A.d.W. zu Berlin Abteilung Biochemie DDR-69 Jena, Beuthenbergstraße 11, German Democratic Republic [2]Organisch-Chemisches Institut der Universität BRD-5300 Bonn, Meckenheimer Allee 168 German Federal Rupubic

Abstract

The effect of deprotonation and alkaline denaturation on the conformation of DNA from various sources has been investigated by optical rotatory dispersion and circular dichroism measurements.

Upon transition to alkaline pH, changes in the optical rotatory dispersion at the characteristic peaks around 228 and 290 nm are observed. The variation of the optical rotations in case of A. T-rich DNA is more pronounced than in case of G . C-rich DNA. For G . C-rich DNA, changes of rotations are mainly observed at pH values beyond 11.5; the transition ranging between pH 11.6 and 11.7. The transition is accompanied by a shift of the "cross-over" point towards longer wavelengths presumably due to deprotonation of guanine residues.

Native DNAs show characteristic differences in their circular dichroism spectra dependent on the G · C content. Increasing the temperature (below the melting region) reveals enhancement of the circular dichroism band of native DNA around 270 nm whereas the opposite effect is found in the denatured state. As a possible explanation an increase of the chirality in the native helical DNA structure or a structure of intermediary character is considered. Titration up to pH 12 or higher produces a drastic increase of the rotational strength around 228 nm as well as changes in the other two circular dichroism-maxima which may be correlated to a diminuition of the chiral and helical structure.

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